REMARKS/ARGUMENTS

I. Support for Claim Amendments

Applicants appreciate the thoughtful comments and suggestions in the Examiner's July 13, 2007 Office Action. Per the Examiner's suggestion on pages 2-3 of the Office Action, Applicants have amended claims 1 and 31-33 to delete the term, "selectively."

Independent claims 1 and 32 have been amended to recite the term "human subject." Support for this amendment may be found in the specification at, *e.g.*, paragraph 229 (describing microarray analysis of human tissue using Affymetrix chips to detect FGFR2, shown in Table 4).

Claims 1 and 31-33 have also been amended to recite the limitation of using a nucleic acid probe that is "at least 95% complementary to SEQ ID NO:1." Support for this claim may be found in the specification at paragraphs 72-76 (describing methods of hybridizing identical and substantially identical nucleic acids); at paragraphs 112-127 (describing hybridization techniques for detecting levels of mRNA expression); paragraph 229 (describing microarray analysis using Affymetrix chips to detect genes identified in Table 4, including FGFR2); and Table 5 (confirming the Affymetrix chip data by RT-PCR measurements of FGFR2 mRNA expression).

Claims 1 and 32 have also been amended to address a possible antecedent basis issue arising from the earlier amendments to the claims. Specifically, the phrase "said polynucleotide" has been deleted and replaced with the phrase, "said subject's FGFR2 mRNA," *i.e.*, the molecule whose diminished expression correlates with major depression disorder, as shown by Applicants. Support for this amendment is found in the specification at, *e.g.*, paragraph 229 (describing microarray analysis using Affymetrix chips to detect genes identified in Table 4 including FGFR2 (pages 1 and 10)); Table 1; Table 2; Table 5; Fig. 4 and Fig. 14 (confirming the Affymetrix chip data by RT-PCR measurements of FGFR2 mRNA expression).

New claims 34 and 35 depend from claims 1 and 32, respectively, and limit the claimed methods to the use of probes which are "at least 95% identical to the full-length complement of SEQ ID NO:1." Support for this claim may be found in the specification at, *e.g.*, paragraphs 72-76 (describing methods of hybridizing identical and substantially identical nucleic acids); and at

paragraphs 112-127 (describing hybridization techniques for detecting levels of mRNA expression).

Thus, no new matter is added by any of the forgoing amendments to the claims.

II. Rejection of Claims 1 and 32 under 35 U.S.C. § 112, paragraph 2 (indefiniteness)

On page 2 of the Office Action, the Examiner rejected claims 1 and 32 under 35 U.S.C. § 112, paragraph 2 as indefinite. Specifically, the Examiner argued that the term "selectively" (as in "selectively associates") was "not defined" and would not be readily understood by one of skill in the art. In the interest of advancing prosecution, Applicants have deleted the phrase from the pending claims. Withdrawal of the Examiner's indefiniteness rejection is earnestly solicited.

III. Rejection of Claims 1 and 31-33 under 35 U.S.C. § 112, paragraph 1 (written description)

On pages 3-5 of the Office Action, the Examiner rejected claims 1 and 31-33 as failing to comply with the written description requirement. Specifically, the Examiner objects to language describing the use of "a nucleic acid probe which is at least 95% complementary to *mRNA encoding FGFR2*." The Examiner argues on one hand that "mRNA encoding FGFR2" includes mRNA "which could be from any species," including species allegedly not disclosed in Applicants' specification. Applicants' have expressly limited the claims to the detection of *human* FGFR2 mRNA to address at least this aspect of the Examiner's argument.

While acknowledging that the specification "reasonably provides support for contacting nucleic acid [*sic*] with a nucleic acid at least 95% identical to SEQ ID NO:1," the Examiner objects to the phrase *"mRNA encoding FGFR2"* because (the Examiner argues) undisclosed sequences could "encode" FGFR2 yet have less than 95% identity to SEQ ID NO:1. As discussed above, Applicants have deleted the offending phrase and the claimed methods now recite the use of a nucleic acid probe that is "at least 95% complementary to SEQ ID NO:1."

Lastly, the Examiner appears to argue that the existence of a relatively "limited sub-genus of mRNAs that encode FGFR2" requires that Applicants limit their claimed methods to probes that are "at least 95% identical to the full-length complement of SEQ ID NO:1." Applicants respectfully submit that the Examiner is misapplying the "written description requirement" in

this particular instance. The Examiner's proposed limitation does not fairly capture the full scope of what Applicants have invented *and described* as their invention.

Applicants acknowledge the Federal Circuit's holding that the enablement and written description requirements are, to some extent, non-overlapping. *See, e.g.*, MPEP 2164, citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) ("the purpose of the 'written description' requirement is broader than to merely explain how to 'make and use'"). However, Applicants' respectfully remind the Examiner that the same panel of CAFC judges held that "the fundamental factual inquiry [for evaluating written description] is whether the specification conveys with *reasonable clarity* to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed." *See id.* at 1563-64. Thus, the state of the art and the knowledge of one skilled in the art is a relevant consideration.[1] Here, the sequences of FGFR2 mRNA are readily available in the art (as well as in Applicants' specification). Similarly, hybridization techniques for measuring expression are routine (and also described in Applicants' specification).

Applicants' specification both enables *and* conveys possession of their claimed invention with *reasonable clarity*. Specifically, Applicants' specification shows that FGFR2 transcription can be measured using probes based on the GenBank M80634, Z71929, M87771 and M87770 sequences for FGFR2. *See, e.g.*, paragraph 229, Table 1, Table 2, Table 4 (pages 1 and 10), and Figure 4. While each of these four mRNA sequences differ, Applicants' specification shows that probes designed to measure expression of the mRNAs yielded the same result, *i.e.*, diminished expression of FGFR2 mRNA (regardless of the isoform) is associated with an increased likelihood of major depression disorder.[2] Applicants' specification also shows that other nucleic acid hybridization-based techniques, *e.g.*, real-time PCR, can be used successfully in their method to achieve the same result. *See, e.g.*, Figure 14. Taking the data and specification as a

[1] In this regard, Applicants note that the Examiner has admitted that Applicants' specification is enabling for "detecting *expression of human FGFR2 receptor nucleic acid* in the dorsolateral prefrontal cortex of a deceased patient and concluding that the patient had major depression disorder." *See* October 24, 2006 Office Action at page 5. At the time of this earlier Office Action, the existence of minor isoforms and/or carboxy-terminal splice variants of mRNA encoding the FGFR2 receptor was evidently (and appropriately) not considered a significant issue by the Examiner.

[2] An Appendix showing the mRNA sequences of M80634, Z71929, M87771, and M87770 is attached.

whole, one skilled in the art would reasonably understand that Applicants possessed the invention as described by the Examiner in the earlier Office Action: a method for "detecting expression of human FGFR2 receptor nucleic acid" and correlating that expression with major depression disorder. Precedent supports this result. *See, e.g., Capon v. Eshhar*, 418 F.3d 1349 (2005) ("when the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh").

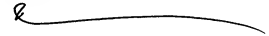
Finally, Applicants note that they are not attempting to claim a broad genus of new nucleic acid *compositions*, nor a broad method for inhibiting the translation of FGFR2 (or one of its isoforms) using nucleic acid probes. If either were the case, the strict treatment given to Applicants' claims under the written description requirement might be warranted. Instead, Applicants' pending claims are diagnostic *method* claims that comprise, in part, well-known and routinely optimizable nucleic acid hybridization techniques using nucleic acid probe sequences that are readily found in the prior art. As noted above, the Examiner previously indicated that Applicants' methods are enabled and, since that time, Applicants have narrowed their claims considerably by, *e.g.*, reciting a discrete FGFR2 reference sequence (*i.e.*, SEQ ID NO.1).

For all the forgoing reasons, Applicants respectfully request withdrawal of the Examiner's written description rejection.

CONCLUSION

Applicants believe all claims now pending in this Application are in condition for allowance. At this stage in prosecution, Applicants have found that any remaining issues are most efficiently resolved by a formal Interview. If the Examiner believes that one or more of the present claims are still not allowable for some reason, Applicants respectfully ask the Examiner to telephone the undersigned at 925-472-5000 so an Interview can be promptly arranged.

Respectfully submitted,



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Fax: 415-576-0300
CJU:jc

61203327 v1

APPENDIX: FGFR2 mRNA SEQUENCES

M80634: mRNA

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Z71929: mRNA

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M87771: mRNA

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LOCUS       HUMKSAMIII               3244 bp    mRNA    linear   PRI 06-JAN-
1995
DEFINITION  Human secreted fibroblast growth factor receptor (K-sam-III)
mRNA,
            complete cds.
ACCESSION   M87771
VERSION     M87771.1  GI:186781
KEYWORDS    K-sam-III; fibroblast growth factor receptor.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 3244)
  AUTHORS   Katoh,M., Hattori,Y., Sasaki,H., Tanaka,M., Sugano,K., Yazaki,Y.,
            Sugimura,T. and Terada,M.
  TITLE     K-sam gene encodes secreted as well as transmembrane receptor
            tyrosine kinase
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 89 (7), 2960-2964 (1992)
   PUBMED   1313574
COMMENT     Original source text: Homo sapiens cDNA to mRNA.
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M87770: mRNA

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LOCUS       HUMKSAMI                4268 bp    mRNA    linear   PRI 06-JAN-
1995
DEFINITION  Human fibroblast growth factor receptor (K-sam) mRNA, complete
cds.
ACCESSION   M87770
VERSION     M87770.1  GI:186779
KEYWORDS    K-sam-I; fibroblast growth factor.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 4268)
  AUTHORS   Katoh,M., Hattori,Y., Sasaki,H., Tanaka,M., Sugano,K., Yazaki,Y.,
            Sugimura,T. and Terada,M.
  TITLE     K-sam gene encodes secreted as well as transmembrane receptor
            tyrosine kinase
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 89 (7), 2960-2964 (1992)
   PUBMED   1313574
COMMENT     Original source text: Homo sapiens brain cDNA to mRNA.
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